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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,228	10/28/2005	David W Morris	PP23370.0003/20366-036US1	4557

55255 7590 04/09/2008

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
04/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,228	MORRIS ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-34,51 and 78-95* is/are pending in the application.

4a) Of the above claim(s) *32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51 and 78-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group XXI, and further election of the human nucleotide sequences corresponding to the gene designated as 07-114, set forth in Table 114 in the reply filed on 2/8/2008 is acknowledged. The traversal is on the ground(s) that groups VIII and XII should be combined and rejoined with group XXI, because the claims in these groups are all based on the common inventive concept that alteration s in expression /levels of the human myosin I sequences are indicative of cancer, and that searching both groups would not constitute an undue burden. This is not found persuasive because the restriction was set forth under PCT Rule 13.1 and in accordance with 37 CFR 1.499 applicable to cases filed under 35 USC 371, which bases the restriction on a finding of a lack of unity with no consideration for burden. The technical feature of the inventions encompassed by claims 32-34 is drugs that alter expression of cancer associated genes, whereas the technical feature of the inventions encompassed by claims 51 and 78-95 is the use of differential expression to diagnose cancer. Thus, the inventions of claims 32-34 read on screening candidate anti-sense, small interfering mRNA or ribozyme compounds for their effect on cancer gene expression, which is an independent and distinct field of endeavor than is the use of cancer gene expression profiles to diagnose cancer. Therefore, the restriction between the two groups is maintained.

The requirement is still deemed proper and is therefore made FINAL.

The amendment filed 2/8/2008 is acknowledged.

Claims 32-34, 51 and 78-95 are pending. Claims 32-34, drawn to non-elected inventions, are withdrawn from consideration.

Claims 51 and 78-95 are examined on the merits.

Information Disclosure Statement

The information disclosure statement and the references cited were considered by the examiner, except for the references lined through. These lined-through references are not in conformance with MPEP 609 37 CFR 1.98 because the citations lack a publication date.

Claim Rejections - 35 USC § 112-second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51 and 94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 51 is indefinite because it recites "a gene which encodes a nucleic acid comprising SEQ ID NO: 777". Genes encode proteins not nucleic acids. Applicants are advised to amend claim 51 to recite "determining the expression of a nucleic acid comprising SEQ ID NO: 777".

Claim 94 is indefinite because it recites a polynucleotide that hybridizes under highly stringent conditions to a nucleotide sequence comprising SEQ ID NO: 777. The specification includes an open definition of what is encompassed by highly stringent conditions, but such an

open definition does not serve to provide the metes and bounds of the claim. Therefore, the scope of the claim is indefinite.

Claim Rejections - 35 USC § 112-first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51 and 78-95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not reasonably provide enablement for methods of diagnosing any and all cancers or for the detection of a propensity towards cancer, comprising the active steps of differential detection of myosin I mRNA, myosin I protein, the detection of differential myosin I mRNA levels, detection of "evidence of differential expression" of myosin I. The basis for this rejection is that the teachings of the specification do not enable the intended use of the claimed methods for the diagnosis of any and all cancers, or for the diagnosis of specific cancers such as colon cancer, lung cancer, pancreatic cancer, ovarian cancer, stomach cancer, breast cancer or prostate cancer.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence

or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The support for methods of diagnosis amounts to a supposition that detection of myosin I mRNA, or myosin I protein correlates with any and all cancer, or with the specific cancers such as colon cancer, breast cancer or prostate cancer, because there are no working examples demonstrating measurements of myosin I mRNA correlate with any cancers.

The art of cancer diagnosis is unpredictable and requires the establishment of certain criteria before the measurement of a marker can be considered a marker for early detection of cancer. For example, Tockman (Tockman, M.S. et al. Cancer Research, (Suppl.) 57: 2711s-2718s, 1992) teaches that the application of a marker for diagnostic purposes requires a provision of a clear definition of the end point for which the candidate protein or gene is to be a marker; an identification of the relevant clinical specimen in which to detect the marker, and the establishment of a range of marker variability (page 2711s, 2nd column).

The claims are also drawn to detecting a propensity to cancer, which is interpreted to read on a method of detecting a predisposition or detecting a precancerous state. The data provided by the specification cannot be extrapolated to such a method of diagnosis, because there is no indication what stage of cancer the samples wee derived from and no data correlating a progression from a precancerous to a cancerous state. With respect to the claims as they relate to detection of differential myosin I protein levels for the purpose of diagnosing cancer, the specification contains no data, and even if mRNA measurements could be used to establish that differential mRNA levels could be used for the diagnosis of cancer, this data cannot be

extrapolated to the use of protein measurements for the diagnosis of cancer. Changes in mRNA levels cannot be predictably associated with changes in protein levels. For example, many proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Thus, given the state of the art as reviewed above, the differential expression of mRNA in tumor cells cannot be used as a basis for the proposition that detection of the claimed polypeptides may be used for detection of tumor cells, because the specification has not correlated the expression of the claimed polypeptides with the treatment or diagnosis of a disease.

Therefore, further research would be required for one of skill in the art to practice the invention for the purpose of using the claimed methods for the diagnosis of cancer or for determining if an individual has a propensity to develop cancer, because neither the specification

nor the prior art has established that myosin I protein, or mRNA levels is associated with a cancer phenotype. The further research that would be required to practice the claimed invention would be undue experimentation because it would require first establishing whether changes in myosin I protein, or mRNA levels is in fact associated with a specific type of cancer, which is research directed to an unpredictable conclusion. This is differentiated from the situation in Wands where the further research was in the realm of routine experimentation to screen for hybridomas that bound to a specific antigen, where the likelihood was extremely high that a monoclonal antibody could be made once one of skill in the art was in possession of a given antigen.

Claims 78-80, 82-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods where the expression product that is detected is an mRNA having a sequence of SEQ ID NO: 777, does not reasonably provide enablement for methods where the expression product that is detected is an mRNA having a sequence at least 98% identical to SEQ ID NO: 777, 95% identical to SEQ ID NO: 777, or is greater than about 75% in overall homology to SEQ ID NO: 777. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Even if the prior rejection under 112, 1st paragraph is overcome, the following rejection will be applied. The broadest claim is drawn to a method for diagnosing cancer comprising detecting evidence of differential expression of myosin I in a patient sample, wherein evidence of differential expression indicates that the patient has cancer. The specification, at page 19,

paragraph 0065, teaches that a nucleic acid is a "CA nucleic acid" if the overall homology of the nucleic acid sequence is greater than about 75% to one of the nucleic acid of Tables 1-128. Therefore, the broadest claim may be interpreted as a method for diagnosis of cancer comprising detecting evidence of differential expression of a sequence having greater than about 75% overall homology to SEQ ID NO: 777.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Because of the broadly recited claims, the methods read on the detection of mutations of myosin I and the detection of mutations for the detection of cancer or for the assessment of risk associated with developing cancer. The specification provides no working examples indicating that mutations of myosin I are known, or that any type of mutation is known to be associated with any type of cancer. Therefore, the specification appears to present nothing more than invitation to research to find out whether mutations exist which may be correlated with a cancer phenotype. This situation appears to be analogous to the situation in Brenner v. Manson (148 USPQ 689 (1966) in which the patent protection was sought for compounds having structures that were similar to a compound with a known utility. The courts concluded that "a patent is not a hunting license…[i]t is not a reward for the search, but compensation for its successful conclusion." In the instant case, even if applicant's establish that detection of mRNA having the

sequence of SEQ ID NO: 777 is useful for the diagnosis of cancer, this will not enable the claimed methods because the claimed methods include those that comprising the detection of mRNA having a sequence that is greater than 75% in overall homology to SEQ ID NO: 777, and the specification has not provided any data or line of reasoning to demonstrate that sequences having this variability in nucleic acid homology to SEQ ID NO: 777 are associated with any type of cancer.

Claims 78-81, 82-92, 94 and 95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification fails to describe the genus of mRNA expression products of myosin I that have greater than 75% sequence identity to SEQ ID NO: 777, or polynucleotides that hybridize under highly stringent conditions to a nucleotide sequence comprising SEQ IDN O: 777, and that are also diagnostic of cancer or diagnostic for a specific cancer. Therefore, the specification lacks adequate written description for the broadly claimed methods.

As discussed above, the specification fails to provide an enabling disclosure for the broadly claimed methods of diagnosing cancer by the detection of differential expression of myosin I, where this is broadly interpreted as reading on methods where differential detection of mRNA having a sequence that is greater than 75% in sequence homology with SEQ ID NO: 777.

The specification fails to provide adequate written description of the genus of myosin I expression products that are diagnostic of cancer.

For a claim drawn to a genus, the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (see Official Gazette 1241 OG 174, January 30, 2001). In the instant case, there is substantial variation in the genus for the broad claims, because expression products of myosin I may be interpreted as having greater than 75% sequence identity to SEQ ID NO: 777. For the narrower claims that recite 98% or 95% sequence identity, the specification also fails to provide support because there is not even one representative species of diagnostic mRNA product that has been shown to be diagnostic of any type of cancer. Therefore, applicant does not appear to be in possession of the broadly claimed methods.

Claims 83-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment filed 2/8/2008 introduces new matter into the specification as originally filed.

The claims are drawn to detection of evidence of differential expression, whereas the original claims and the originally filed specification are drawn to measuring actual differential expression. Thus, the amendment filed 2/8/2008 introduces new matter by broadening the scope of the claims from what was originally contemplated. The amended claims are broader in scope than the originally filed claims because detecting evidence of differential expression may include measuring such things as flux through a pathway or measuring genetic mutations. There is no explicit contemplation in the originally filed claims or specification of measuring evidence of differential expression, and because there is no definition of the scope of the phrase, broadly interpreted, measuring evidence of instead of actual differential expression implies indirect measurements for which the specification has no support with respect to methods of cancer diagnosis. Therefore, one of skill in the art would not find that applicant was in possession of the inventions as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 83-87 and 91-93 are rejected under 35 U.S.C. 102(e) as being anticipated by Venter (US 6,821,339; issued Nov. 2, 2004; effective filing date is Oct. 20, 2000).

Venter teaches SNP sequences and teaches in particular SEQ ID NO: 4522, which is identical to instant SEQ ID NO: 777. Venter teaches that detection of the provided SNP sequences, of which SEQ ID NO: 4522 is one, allows the detection of diseases. Because SEQ ID NO: 4522, which is identical to SEQ ID NO: 777, is a SNP sequence, detection of this sequence constitutes detection of evidence of differential expression of myosin I, meaning that in an individual, if SEQ ID NO: 4522 is detected then that individual expresses a variant of myosin I. Venter teaches detection of mRNA expression and protein expression (see column 27, lines 41-64, and column 33, lines 18-57). Thus, Venter teaches the methods as claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
March 31, 2008

/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643